Modified PTO/SB/33 (10-05)

PRE-APPEAL BRIEF REQUEST FOR REVIEW	Docket Number Q94633	
Mail Stop AF Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Application Number 10/577,154	Filed April 26, 2006
	First Named Inventor KITAZONO, Eiichi	
	Art Unit 1623	Examiner Bahar Schmidtmann

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal

The review is requested for the reasons(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

☑ I am an attorney or agent of record.
Registration number 33,725

/Bruce E. Kramer/
Signature

Bruce E. Kramer
Typed or printed name

(202) 293-7060
Telephone number

September 7, 2010
Date

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

KITAZONO, Eiichi, et al.

Docket No: Q94633

Appln. No.: 10/577,154

Group Art Unit: 1623

Confirmation No.: 1395

Examiner: Bahar Schmidtmann

Filed: April 26, 2006

For: HYALURONIC ACID COMPOUND, HYDROGEL THEREOF AND JOINT TREATING MATERIAL

PRE-APPEAL BRIEF REQUEST FOR REVIEW

MAIL STOP AF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Pursuant to the Pre-Appeal Brief Conference Pilot Program, and further to the Examiner's Final Office Action dated March 4, 2010, Applicant files this Pre-Appeal Brief Request for Review. This Request is also accompanied by the filing of a Notice of Appeal.

Applicants turn now to the rejection at issue:

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katsukiyo et al. (US Patent No. 5,733,892) in view of Shigehisa et al. (JP 06-072893).

Applicants respectfully submit that the present invention is not obvious over the cited art, and request that the rejection be reconsidered and withdrawn in view of the following remarks.

1. The present invention is directed to a hyaluronic acid compound represented by the recited formula (1), that is, a combination of hyaluronic acid and phosphatidyl ethanolamine as

set forth in claim 1. The desired object, that is, the protection of a joint can be attained by selecting a hyaluronic acid compound having numerical values specified in claim 1.

Both Katsukiyo and Shigehisa fail to disclose or suggest the above hyaluronic acid compound of the present invention and a joint protection function which is attained by the compound.

The joint injectable preparation of the present invention is considered to develop a joint protection function by a hydrogel having high viscoelasticity, i.e., a shock absorbing function. That is, this function differs from the suppression of cancer metastasis in Katsukiyo and the treatment of rheumatoid arthritis in Shigehisa in mechanism. In this regard, it is submitted that one of ordinary skill in the art would not have modified Katsukiyo (directed to the suppression of cancer metastasis) based on the disclosure of Shigehisa (directed to the treatment of rheumatoid arthritis) in view of the difference in function.

As understood from the passage "The amount of the active ingredient in the medical preparation may be varied within the range of from 1 to 90 % by weight based on the weight of the carrier" (column 36, lines 42-45) after a description of the preparation of Katsukiya cited by the Examiner (page 5, lines 11-14 of the final Office Action), the amount of the active ingredient may be 1 wt%. It can be understood from this that the disclosed pharmacological effect of the active ingredient is expected, and the injectable preparation is merely described as one of a large number of dosing preparations enumerated in Katsukiyo.

In contrast to this, the compound of the present invention must have a high elastic modulus (must be able to be administered) when it is prepared as a hydrogel and thereby can develop a joint protection function.

2. As the Examiner indicates, Katsukiyo does not disclose the embodiment of phosphatidyl ethanolamine where the acyl groups are unsaturated. Further, Katsukiyo also fails to disclose that a joint protection function is achieved by the hyaluronic acid compound of the present invention having the above embodiment.

3. Shigehisa discloses "hyaluronic acid, chondroitin, chondroitin sulfate (A, C, D, E, K), chondroitin polysulfate, dermatan sulfate, heparin, heparan sulfate, keratan sulfate, keratin polysulfate" as glycosaminoglycans (GAG) which are raw materials for the production of a lipid-bound glycosaminoglycan (paragraph (0020]) and also "phosphatidyl ethanolamine, phosphatidyl serine, phosphatidyl threonine, ethanolamine plasmagene, serine plasmagene. lysophosphatidyl choline, lysophosphatidyl inositol" as phospholipids out of lipids and teaches that "the chain length and unsaturation degree of the acyl group are not particularly limited but examples of the acyl group include palmitoyl (hexadecanoyl) and stearoyl (octadecanoyl)" as for the acyl group in the lipid. Further; examples of a reaction for producing the lipid-bound GAG through bonding between the raw material GAG and a lipid include nine reactions (a) to (i) as described in the paragraph [0018].

The hyaluronic acid compound in claim 1 of the present application is obtained only by selecting hyaluronic acid as GAG and phosphatidyl ethanolamine as a lipid from the above raw materials enumerated in Shigehisa, further selecting an acyl group having an alkenyl group with

10 to 28 carbon atoms which is not even described in Shigehisa and carrying out a reaction (e) out of the above reactions to bond these.

It is defined in claim 1 of the present application that the hyaluronic acid compound further has a group (formula (1)'-a) derived from phosphatidyl ethanolamine having an alkenyl group with 10 to 28 carbon atoms in the acyl group in an amount of 1 to 100 % of the total of all the carboxyl groups of hyaluronic acid.

When the above hyaluronic acid compound of the present invention has the above group represented by the formula (1)'-a in an amount of 1 to 100 % of the total of all the carboxyl groups of hyaluronic acid, it can form a hydrogel having a high elastic modulus of not less than 200 Pa and is useful for the treatment of a knee cartilage damage (see page 7, lines 18-21 of the present application).

Shigehisa teaches that lipid-bound GAG has the effect of suppressing the extension of pannus which causes cartilage destruction as an anti-rheumatic agent for improving the symptoms of rheumatism (RA) and the effect of easing the inflammation reaction of a synovial membrane and is used as an anti-rheumatic agent having little toxicity and few side-effects (see paragraph [0008]) but does not disclose that the lipid-bound GAG is effective for the treatment of cartilage damage of a joint such as a knee.

As described above, the hyaluronic acid compound in claim 1 of the present application is a novel and unobvious compound having a specific structure which is not disclosed by Katsukiyo and Shigehisa and has an excellent function and effect, that is, a joint protection

function and the effect of treating cartilage damage of a joint such as a knee which are not disclosed by Katsukiyo and Shigehisa.

4. The Advisory Action describes on page 8, lines 2-3 that "it is clear that they have a high elastic modulus when prepared as a hydrogel."

However, Katsukiyo et al. and Shigehisa et al. fail to suggest that not only the compound of the present invention but also the compounds having close structural similarity to the compound instantly claimed have a high elastic modulus when prepared as a hydrogel.

The present invention has been accomplished based on the finding that the elastic modulus drastically increases unexpectedly when the side chain of hyaluronic acid is modified by the specific phosphatide as shown in Table 1 in the present application. A joint protection function is obtained by this high elastic modulus and cannot be expected from the cited references.

Therefore, Applicants submit that the invention of claims 1-8 is not obvious over Katsukiyo in view of Shigehisa, and withdrawal of this rejection is respectfully requested.

Respectfully submitted,

/Bruce E. Kramer/
Bruce E. Kramer
Registration No. 33,725

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: September 7, 2010